

**University Hospitals
Health System**

University Hospitals
of Cleveland , 266 '99 DEC -8 10 28

November 26, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: 21 CFR Parts 600 et al: Requirements for Testing Human Blood Donors for Evidence of Infection Due to Communicable Disease Agents, Proposed Rule [Docket No. 98N-0581]

To Whom It May Concern:

The proposed rule listed above, described on pages 45340-45355 of the Federal Register, August 19, 1999, would apparently mandate transfusion-transmitted disease testing of all units of blood intended for transfusion *including autologous units*. This rule would essentially negate the current practice in many hospitals of not testing autologous units for markers of infectious disease provided they are both collected and transfused in the same facility. The presumed rationale for this proposed rule, discussed during the June 1994 Blood Products Advisory Committee meeting is to (1) reduce the possibility of erroneous transfusion of an infectious autologous unit; (2) protect health care workers who handle infectious blood and, (3) be a step toward uniform handling, i.e. the standardization of allogeneic and autologous blood units.

As I have indicated previously on multiple occasions in writing and in national presentations the proposed new rule and the assumptions, upon which it is based, are, in my opinion, flawed. As I have previously noted (Yomtovian R. Mandatory infectious disease marker testing of autologous blood - a flawed proposal. Transfusion 1996; 36:85-86) the possibility that infectious disease marker testing will reduce the risk of inadvertent transfusion of infectious autologous units has not been substantiated. In an American Association of Blood Banks anonymous survey of 1829 institutions (AABB position on testing of autologous units. Association Bulletin 95-4, Bethesda: American Association of Blood Banks, May 10, 1995:3-4), cited repeatedly in this Federal Register text to support promulgation of the new proposed rule, the erroneous transfusion of an autologous unit to an unintended recipient was reported by 22 facilities. **However, as Chairperson of the Autologous Transfusion Committee of the American Association of Blood Banks during the time this anonymous survey was authored, it is important to emphasize, critical to the issue of improving transfusion safety, that there was no apparent correlation identified, in participating facilities, between erroneous transfusion and the performance of**

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infectious disease marker testing of these units before transfusion. Institutions performing infectious disease marker testing on autologous units made no fewer errors than institutions not performing testing. It is thus unclear to me how promulgation of this new proposal will increase transfusion safety. In addition, in no instance was an erroneously transfused unit reported to be positive for an infectious disease marker. This is not surprising since, as calculated (Menitove JE. Handling the infectious autologous unit. Presented as part of the workshop entitled, "Current issues created by the implementation of autologous and directed donor programs" American Association of Blood Banks 46th Annual Meeting, Miami, FL, October, 1993) the risk of simultaneously transfusing an erroneous unit that is also infectious marker positive would be a multiple of each risk separately. Thus, the risk of erroneously transfusing an autologous unit to an incorrect patient that is also positive for HIV or HCV or HBV is less than 1 in 3,000,000 (the risk for HIV is estimated at 1 in 40,000,000 to 1 in 1/100,000,000). Furthermore, and of particularly critical importance, since medical, legal, and ethical interests do not warrant the mandatory destruction of infectious disease marker positive units (Yomtovian R, Kelly C, Bracey AW et al: Procurement and transfusion of human immunodeficiency virus-positive or untested autologous blood units: issues and concerns: a report prepared by the Autologous Transfusion Committee of the American Association of Blood Banks, Transfusion 1995; 35:353-361) contaminated units will continue to be present in some inventories; and, the fact that those units are present in inventories results in a risk, albeit tiny, for error. **Accordingly, it is not infectious disease marker testing that is needed, but rather careful attention to transfusion practices, promulgated and enforced at each facility, handling these and all units of blood.**

Certainly, autologous units are and should continue to be distinctive in appearance as evidenced by their unique green labels. Furthermore, units that are untested for infectious disease markers should contain, in my view, not only a statement that they are untested but and indication that these represent a biohazard; i.e. untested units should be assumed to be positive for markers of infectious disease. While this won't prevent inadvertent erroneous transfusion, neither will mandatory testing. Furthermore, mandatory testing will not only increase costs at a time when blood banks are being asked to absorb other costly mandates, it might be counterproductive. Mandating testing, as noted above, will not prevent errors. Only careful attention to transfusion practices will prevent the erroneous transfusion of a "hot" (infectious disease marker positive) autologous unit. However, mandatory testing may give a false sense of increased protection, which may result in reduced attention to proper transfusion practices. (Yomtovian R. Autologous Transfusion Complications. In: Popovsky MA, ed. *Transfusion Reactions*, Bethesda, MD: AABB Press, 1996: pages 237-280.) And, certainly there will be fewer resources available to devote to improvements in transfusion practice as limited resources are applied increasingly applied to testing.

Finally, mandatory testing will likely mean that individuals who otherwise qualify for autologous donation and transfusion will be denied this service. To mention an actual example, in our facility in over 10 years we have collected and transfused over 5,000 autologous units untested for infectious disease markers without incident. During this same time we have also received tested autologous units from outside suppliers. In one instance, a reconstructive facial surgery was denied to a young man because of a false positive HIV result, which could not be resolved in time to proceed with the surgery. The

surgery was never rescheduled at our facility because of fear and misunderstanding of the meaning of falsely positive HIV serology results denying this patient needed surgery at our facility.

The possibility of protecting healthcare workers from accidental transmission of disease of infectious disease marker testing is unproven, costly and contradictory to the notion of universal blood precautions. The paradigm of universal precautions, widely applied and endorsed, is predicated on the careful and uniform handling of all blood samples as though each is infectious. Mandating testing to identify infectious autologous units sets an unfortunate double standard.

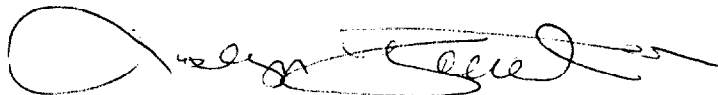
The desire to force autologous and allogeneic practices into an identical pigeonhole to reduce errors fails to account for inherent and fundamental differences between these modalities. Autologous blood donors are patients and cannot be held to the same guidelines as allogeneic donors. An inability to differentiate and separate these these classes of donors may lead to a growing number of instances, as per the example cited above, in which the medical benefits of autologous blood are denied.

Mandatory infectious disease marker testing adds both direct and indirect costs for testing and administrative complexity. Since reimbursement for autologous transfusion is already inadequate (Yomtovian R, Kruskal MS, Barber JP. Current concepts review. Autologous-blood transfusion: the reimbursement dilemma. J Bone Joint Surg [Am] 1992; 74:1265-72), it is likely that these added costs will worsen the reimbursement dilemma for those facilities that omit infectious disease marker testing. Indeed, there is already a hint, notwithstanding the example cited above, that infectious disease marker testing may be a barrier to autologous transfusion practice. In institutions utilizing infectious disease marker tested autologous units, the autologous transfusion rate is 2.4%, while in institutions utilizing infectious disease marker untested units, the rate is 3.7% ($p < 0.001$) (Renner SW, Howanitz PJ, Bachner P. Preoperative autologous blood donation in 612 hospitals: a College of American Pathologists' Q-Probes study of quality issues in transfusion practice. Arch Pathol Lab Med 1992;116:613-619).

As indicated in the text accompanying the proposed new rule, improvement in the safety of autologous transfusion is of paramount importance. Unfortunately, the application of mandatory infectious disease marker testing is unlikely to achieve this goal, but will add significant expense and create bottlenecks. The end result might well be a dismantling of the safest form of transfusion therapy ---- autologous transfusion.

Thank you for your attention. I am confident your agency will reconsider the proposal to mandate infectious disease marker testing of autologous units collected and transfused in the same facility. Instead, I hope the agency will encourage the development and promulgation of strategies to reduce the potential for transfusion errors.

Sincerely,

A handwritten signature in black ink, appearing to read 'Roslyn Yomtovian', with a large, stylized loop at the beginning and a horizontal line extending to the right.

Roslyn Yomtovian, M.D.

Director, Blood Bank-Transfusion Medicine Service, University Hospitals of Cleveland
Associate Professor, Case Western Reserve University School of Medicine, Department
of Pathology

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